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Influence of gestogenic contraceptive pills on vaginal candidosis

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The use of antiovulatory contraceptive pills has increased rapidly in recent years and the World Health Organisation estimates that they are being taken by more than 20 million women throughout the world. In Britain, the Committee on the Safety of Drugs has stated that contraceptive pills are employed by over a million and a half women at the present time. The increasing use of these preparations has been followed by a corresponding increase in the number of side-effects attributed to them; some have been serious and a number of deaths have been reported. This paper presents further information about the relationship between gestogenic contraceptive pills and vaginal candidosis. Although this is usually a benign complication, it may lead to distressing symptoms, and on rare occasions to serious systemic manifestations. The condition can be passed to men at sexual intercourse, when it usually results in balanoposthitis.

Candida albicans is a facultative pathogen. Its pathogenicity depends not only on the size of the colonies, but also on the tolerance of the host tissues to it. There is evidence that the mucosa of the mouth, intestines, and vagina can show a marked tolerance to the fungus, whereas it is probable that it usually causes symptoms when found on the skin or elsewhere (Kozinn and Taschdjian, 1966). A change in the tissues or the metabolism of the host may disturb the equilibrium and lead to the development of symptoms.

There is general agreement that the incidence of vaginal candidosis is increasing in many countries and the condition is being diagnosed more frequently (Pumpianski and Sheskin, 1965). *Candida albicans* has now replaced *Trichomonas vaginalis* as the commonest cause of genital symptoms in women and it is probably the pathogen found most frequently in those complaining of vaginal discharge.

For example, at James Pringle House of the Middlesex Hospital in 1965, the ratio of cases of trichomonal vaginitis to cases of vaginal candidosis was two to one amongst all the women complaining of genital symptoms and three to one amongst those complaining specifically of vaginal discharge. By 1969 the ratios had changed completely, so that for all the women with genital symptoms the ratio was one to three and for those complaining of vaginal discharge it was one to two (Table I).

TABLE I *Change in ratio of* Trichmonas *to* Candida

Year	1965	1969
All patients with genital symptoms	2 to 1	1 to 3
Patients with vaginal discharge	3 to 1	1 to 2

Many of the commoner conditions which favour the development of *Candida albicans* in the vagina are well known (Table II). In Britain, the most important are pregnancy, diabetes mellitus, antibiotic therapy, steroid therapy, and the use of antitrichomonal agents. Evidence that gestogenic pills play an important role in the recent increase in incidence of vaginal candidosis has been put forward by a number of authors. Bourg (1964) observed that six of sixty patients taking contraceptive pills developed vaginal candidosis. Gardner (1965) stated that half his patients with vaginal candidosis were using these

TABLE II *Factors favouring the development of candidosis*

1. Physiological factors, *e.g.* pregnancy, early infancy
2. Skin diseases, maceration, and wounds
3. Endocrine disorders, *e.g.* diabetes mellitus, hypothyroidism, hypoparathyroidism, Addison's disease, and pancreatitis
4. Undernourishment
5. Disorders of absorption
6. Antibiotic therapy
7. Steroid therapy
8. Blood dyscrasias, *e.g.* acute leukaemia, agranulocytosis, and aplastic anaemia
9. Surgical operations
10. Malignant diseases and cytotoxic agents
11. Antitrichomonal agents
12. Contraceptive pills

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preparations and thought that the recent increase in the incidence of the condition was almost entirely due to antiovulatory contraceptives. Walsh, Hildebrandt, and Prystowsky (1965) demonstrated *Candida* in twenty-two of twenty-four patients using contraceptive pills and Yaffee and Grots (1965) found that they could cure their patients of vaginal candidosis only by discontinuing the pills. Porter and Lyle (1966) treated thirteen patients with candidosis, who were using oral contraceptive pills; most of them required two or three courses of nystatin to clear the condition and in three cases it was necessary to discontinue the pills before cure could be achieved.

Catterall (1966) described six women whose symptoms first appeared about 9 months after starting to take contraceptive pills. He also described four men who presented with balanoposthitis due to *Candida albicans;* all of their sexual partners were found to have vaginal candidosis and had been taking pills for 6 to 12 months. These findings were confirmed by Rieth (1967), who described penile symptoms after coitus in a man whose partner was found to have vaginal candidosis and had been taking pills for 10 months.

However, Morris and Morris (1967, 1969) were unable to demonstrate a relationship between oral contraceptives and the incidence of *Candida albicans* in the vagina or any other change in the vaginal flora.

Gardner (1965) believed that the hormonal changes induced by gestogenic contraceptive pills corresponded closely to those of pregnancy and regarded the resulting state of the patient as 'pseudopregnancy'. As in a true pregnancy the glycogen content of the vaginal mucosa was increased. This led to the growth of lactobacilli, which converted the glycogen into lactic acid. The increased glycogen, the presence of lactic acid, and the change in the pH of the vagina were thought to promote the growth of *Candida albicans* and the vagina was considered to become the ideal culture medium for *Candida.* Cohen (1969) demonstrated that women with a low vaginal pH were more liable to infection and attributed this to excessive desquamation of the epithelium causing a break in the continuity of the vaginal mucosa.

Wynn and Doar (1966) demonstrated a reduction in glucose tolerance in women taking oral contraceptive pills. They later suggested that the impaired glucose tolerance was a type of 'steroid diabetes' caused by elevated plasma cortisol levels secondary to the oestrogen component of the oral contraceptive (Wynn and Doar, 1969). They were unable to predict which women were likely to develop serious impairment of glucose tolerance and could only speculate whether the impaired glucose tolerance and raised plasma insulin levels might increase the rate of development of clinical diabetes mellitus and of atherosclerosis. Spellacy (1969) reviewed the evidence of impaired oral and intravenous glucose tolerance and the changes in the circulating levels of other compounds related to glucose tolerance, including insulin, non-esterified fatty acid, and pyruvate.

An analysis of the records of 200 women attending James Pringle House at the Middlesex Hospital and found to have vaginal candidosis, showed that 99 were taking contraceptive pills, 22 had recently been prescribed broad-spectrum antibiotics, twelve were pregnant, and ten had taken a course of antitrichomonal agents, shortly before the diagnosis of candidosis was made. Two patients were found to have diabetes. No cause could be found for the condition in 55 patients (Table III).

TABLE III 200 *patients with vaginal candidosis*

Contraceptive pills	99
Broad-spectrum antibiotics	22
Pregnancy	12
Antitrichomonal agents	10
Diabetes	2
Cause unknown	55
Total	200

Of the factors known to favour the development of candidosis, pregnancy, diabetes mellitus, recent antibiotic therapy, antitrichomonal agents, and oral contraceptive pills are probably the most important in the aetiology of vaginal candidosis. The balance of clinical evidence suggests that there is a relationship between the use of gestogenic pills and the development of vaginal candidosis and this association is supported by the experimental work indicating an alteration in glucose metabolism, an increase in the serum binding of insulin, and an abnormal glucose tolerance curve, as well as the changes in the pH of the vagina.

Although the condition can usually be controlled by nystatin pessaries, in some cases it is necessary to stop the use of the pill to produce relief from the symptoms and to cure the patient.

Summary and conclusions

(1) A review of the literature indicates that there is probably a causal relationship between the use of gestogenic contraceptive pills and the development of vaginal candidosis.

(3) This view is supported by recent experimental evidence of changes in glucose metabolism and in vaginal pH in women taking contraceptive pills.

(3) A change in the ratio of patients with trichomonal vaginitis and vaginal candidosis in recent years

and an analysis of causative factors amongst women with vaginal candidosis suggest that oral contraceptive pills are now the commonest cause of the condition.

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